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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: DENATURAT STABLE AND/OR PROTEASE RESISTANT, CHAPERONE-LIKE OLIGOMERIC PROTEINS, POLYNUCLEOTIDES ENCODING SAME, THEIR USES AND METHODS OF INCREASING A SPECIFIC ACTIVITY THEREOF

(57) Abstract: Novel denaturant-stable, protease resistant, homo-oligomeric proteins, also referred to herein as stable proteins (SPs), having chaperone-like activity; methods of production and purification of SPs; nucleic acids encoding SPs; methods of isolating nucleic acids encoding SPs; antibodies recognizing SPs; the use of SPs for stabilizing, refolding, repairing, preventing aggregation and de-aggregating macromolecules such as proteins; fusion proteins including SPs; nucleic acid constructs encoding the fusion proteins; and their uses in a variety of methods and applications.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL03/00723

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 15/29,15/82; A01H 5/00
US CL : 435/320.1,419; 536/23.6; 800/298

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 435/320.1,419; 536/23.6; 800/298

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Continuation Sheet

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P --- Y,P	WANG et al. Characterization of sp1, a stress-responsive, bioling soluble, homo-oligomeric protein from aspen. Plant Physiology. October 2002, Vol. 130, pages 865-875, especially page 866 Figure 1, page 867 Figure 2, page 871 Figure 8.	1-4, 6, 9-13, 16-19, 21, 24-28, 31-34, 36, 39-43 --- 5, 7-8, 14-15, 20, 22-23, 29-30, 35, 37-38, 40-45
X	Database GenBank on STIC, National Center for Biotechnology Information (Bethesda, MD, USA), Accession No. M18538. BRADSHAW et al. Populus x generosa pop3 peptide mRNA complete cds, gene sequence, 30 November 2000.	1-4, 6-13, 16-19, 21-28, 31-34, 36-43 --- 5, 14-15, 20, 29-30, 35, 44-45
X	WANG et al. Plant tolerance to water and salt stress: the expression pattern of a water stress responsive protein (BspA) in transgenic aspen plants. Plant Biotechnology and in vitro biology in the 21st century. 1999, Kluwer Academic Publishers, Dordrecht, A. Altman et al. (eds.), pages 561-565, the entire article.	1-6, 9-13, 16-21, 24-29, 31-36, 39-43

☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

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28 July 2004 (28.07.2004)

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INTERNATIONAL SEARCH REPORT

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LIU et al. Characterization of the Xp21-23 region in the wood lemming, a region involved in XY sex reversal. Journal of Experimental Zoology. 2001, Vol. 290, pages 551-557, especially page 552 column 2 first full paragraph, page 554 column 2 lines 29-36.	15, 30, 45

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IL03/00723

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claim Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-45, directed to SEQ ID NOS:1 and 2

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I-VI, claim(s) 1-45, drawn to an isolated nucleic acid, a cell, an organism, and a method of isolating a gene. (Group I is directed to a nucleic acid of SEQ ID NO:1 encoding SEQ ID NO:2, Group II is directed to a nucleic acid of SEQ ID NO:5, Group III is directed to a nucleic acid of SEQ ID NO:6, Group IV is directed to a nucleic acid of SEQ ID NO:34 encoding SEQ ID NO:35, Group V is directed to a nucleic acid of SEQ ID NO:39, Group VI is directed to a nucleic acid of SEQ ID NO:40)

Group VII-XII, claim(s) 46-50, 53, 56-60, 63, 66-70, 73 and 76-77, drawn to an isolated polypeptide, a method of using a polypeptide to prevent protein aggregation, and a method of isolating a protein. (Group VII is directed to a protein of SEQ ID NO:2 encoded by SEQ ID NO:1, Group VIII is directed to a protein encoded by SEQ ID NO:5, Group IX is directed to a protein encoded by SEQ ID NO:6, Group X is directed to a protein of SEQ ID NO:35 encoded by SEQ ID NO:34, Group XI is directed to a protein encoded by SEQ ID NO:39, Group XII is directed to a protein encoded by SEQ ID NO:40)

Group XIII, claim(s) 51-52, 61-62 and 71-72, drawn to an antibody and a method of using an antibody to isolate a gene.

Group XIV, claim(s) 54, 64 and 74, drawn to a method of using a polypeptide to de-aggregate protein.

Group XV, claim(s) 55, 65 and 75, drawn to a method of using a polypeptide to stabilize a protein against denaturing conditions.

Group XVI, claim(s) 78, drawn to a method of isolating a gene.

Group XVII, claim(s) 79, drawn to a method of isolating a gene.

Group XVIII, claim(s) 80, drawn to a method of isolating a nucleic acid.

Group XIX, claim(s) 81, drawn to a method of identifying a nucleic acid.

Group XX, claim(s) 82, drawn to a method of isolating a nucleic acid.

Group XXI, claim(s) 83, drawn to a method of isolating a protein.

Group XXII, claim(s) 84-87, drawn to a fusion protein.

Group XXIII, claim(s) 88, drawn to a method of immunization.

Group XXIV, claim(s) 89, drawn to a method of protecting an enzyme preparation from reduction in enzymatic activity.

Group XXV, claim(s) 90, drawn to a method of repairing at least a portion of lost enzymatic activity of an enzyme preparation.

Group XXVI, claim(s) 91, drawn to a method of administering a polypeptide to an animal having an immune system.

Group XXVII, claim(s) 92-94, drawn to a transgenic plant and a method of engineering a plant.

Group XXVIII, claim(s) 95, drawn to a method of increasing cell migration.

Group XXIX, claim(s) 96, drawn to a method of accelerating wound healing.

Group XXX, claim(s) 97, drawn to a method of inducing wound healing.

Group XXXI, claim(s) 98, drawn to a method of strengthening hair, nail or skin.

Group XXXII, claim(s) 99, drawn to a method of grooming the hair, nail or skin.

Group XXXIII, claim(s) 100-102, drawn to a pharmaceutical composition.

Group XXXIV, claim(s) 103-104, drawn to a method of isolating a protein.

Group XXXV, claim(s) 105-106, drawn to a method of treating a disease.

Group XXXVI, claim(s) 107-108, drawn to a method of increasing a binding avidity of a binding molecule.

Group XXXVII, claim(s) 109-113, drawn to a hetero complex.

Group XXXVIII, claim(s) 114-129, drawn to an isolated protein.

Group XXXIX, claim(s) 130, drawn to a method of increasing a specific activity of a protein.

Group XL, claim(s) 131, drawn to a method of increasing a specific activity of a protein.

The inventions listed as Groups I-XL do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The technical feature linking Groups I-XL is a boiling stable protein. However, a boiling stable protein is obvious or anticipated over PELAH et al. (Tree Physiology, 1995, Vol. 15, pages 673-678). Therefore, the technical feature linking the inventions of Groups I-XL does not constitute a special technical feature as defined by PCT Rule 13.2, because it does not define a contribution over the prior art. Furthermore, the special technical feature of each group of invention is the particular product and/or the particular method of making and/or using that product as set forth in the claims, as the products of groups I-XIII, XXII, XXVII, XXXIII, XXXVII and XXXVIII are different from each other, as are the methods of groups I-XXI, XXIII-XXXII, XXXIV-XXXVI, XXXIX and XL.

Continuation of B. FIELDS SEARCHED Item 3:
STN (agricola, biosis, biotechno, caba, caplus, medline, uspatfull): inventor names, aspen, Populus, bspA, sp1, pop3, stable, chaperonin, expression, library, hybridization; STIC sequence search for SEQ ID NOS: 1 and 2.